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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/466,035	12/17/1999	MATTI SALLBERG	930049.458C1	9697

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EXAMINER	
WEHBE, ANNE MARIE SABRINA	
ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
12/12/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/466,035	SALLBERG ET AL.	
	Examiner	Art Unit	
	Anne Marie S. Wehbe	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,12,13 and 26-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,12,13 and 26-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/22/07 has been entered. Applicant's amendment and response filed on 10/22/07 has also been entered. Claims 6-11, 14-25, and 30 are canceled. Claims 1-5, 12-13, and 26-29 are pending in the instant application. An action on the merits follows.

It is noted that those sections of Title 35, US code not included in this action can be found in the previous office action.

37 CFR 1.121

The amendment to the claims filed on 10/22/07 is objected to under 37 CFR 1.121 (c). Specifically, claims 27-29 are listed as currently amended; however, the claims lack any marking to indicate changes from the previous claim set filed on 7/10/06 and further do not appear to differ from previously pending claims 27-29. Thus, the claim identifier for these claims is incorrect. In the interests of compact prosecution, this amendment has been entered. However, applicant is advised that future claim amendments which do not adhere to the requirements of 37

CFR 1.121(c) will not be entered and a letter of non-compliant amendment under 37 CFR 1.121 will be mailed to the applicant.

Information Disclosure Statement

Applicant's IDS filed on 10/22/07 has been considered by the examiner. An initialed copy is attached to this office action.

Applicant's amendments to the claims has necessitated the following new grounds of rejection under 35 U.S.C. 112, second paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-5, 12-13, and 26-29 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 has been amended to recite administering a "non-replicating vector construct... wherein the vector construct is selected from the group consisting of retroviral vectors, alphavirus vectors, parvovirus vectors, and eukaryotic layered vector initiation system vectors...". The addition of the term "non-replicating" to the initial recitation of "vector construct" renders the claim indefinite as the list of vector constructs recited in the claims are not limited to non-replicating vectors. Thus, the metes and bounds of the claim are unclear.

Claim Rejections - 35 USC § 103

The rejection of claims 1-5, 12-13, and 26-30 under 35 U.S.C. 103(a) as being unpatentable over WO 95/07994 (1995), hereafter referred to as Dubensky et al., in view of Hu et al. (1991) AIDS Res. Hum. Retrovir., Vol. 7 (7), 615-620 is maintained over pending claims 1-5, 12-13, and 26-29, claim 30 having been canceled. Applicant's arguments have been fully considered but have not been found persuasive in overcoming the instant rejection for reasons of record as discussed in detail below.

The applicant argues that the cited combination of references does not meet the requirements for establishing obviousness under 103 for the claims as amended, citing *In re Dembicak*, *Graham v. John Deere Co.*, and *KSR Int'l Co. v. Teleflex Inc.* Specifically, the applicant argues that the claims have been amended to recite that the vector is a non-replicating vector and that Hu et al. teaches the use of a prime boost strategy with a replicating vaccinia virus vector such that the skilled artisan would not be motivated to combine the teachings of Hu et al. with those of Dubensky et al. who teaches the use of non-replicating vectors, i.e. alphavirus vectors or layered eukaryotic systems. The applicant explains their argument further stating that since replicating viral vectors exponentially replicate, larger quantities of both the expressed antigen as well as the vector occur in animals vaccinated with replicating vectors versus non-replicating vectors. The applicant further cites Paielli et al. as evidence of the increased viral DNA observed in animals given a replication competent vector versus a replication-defective vector. Finally, the applicant argues that Hu teaches away from

using a non-replicating vector by teaching the advantages of a replicating viral vector in the prime-boost regimen, pointing to the abstract and Tables 1 and 2 of Hu et al.

In response, it is first noted that the rejection of record is based upon an analysis of the claimed invention as set forth in *Graham v. John Deere Co.* The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Regarding the newly added limitation that the vector is "non-replicating", it is first noted that the group of vectors listed in claim 1 are not limited to "non-replicating" vectors. Retroviral vectors, alphavirus vectors, and parvovirus vectors include both replication competent and non-replication competent species, see the new rejection of the claims under 35 U.S.C. 112, second paragraph, above. However, in the interests of compact prosecution, the grounds of rejection as they apply to non-replicating vectors is addressed in view of applicant's arguments.

In response to applicant's arguments, it is not agreed that Hu's use of a "replicating" vaccinia virus teaches away from the use of a "non-replicating" vector, or that the skilled artisan would not have been motivated to use the prime-boost strategy of Hu with the non-replicating vectors taught by Dubensky et al.. It is first noted that Dubensky et al. teaches the use of live recombinant alphavirus to stimulate immune responses which are either replication competent or replication defective. See for example pages 6 and 15 which discuss alphavirus

vectors with modified viral junction regions. These viruses do in fact replicate, they are just attenuated due to the viral junction modification. Further, Dubensky et al. teaches that the layered eukaryotic vector initiation systems comprises as a second layer a replicating construct which includes poxvirus, see pages 8 and 38. Thus, Dubensky et al. provides teachings that the replication status of the immunizing alphavirus or layered eukaryotic vector initiation system does not affect the ability of these expression systems to express a heterologous antigen and induce an antigen specific immune response. In addition, it is noted that Dubensky in pages 148-151 teaches non-replicating sindbis vectors encoding HBV or HIV antigens and the use of multiple administration of the vector to induce immune responses, i.e. prime and boost using the same vector. Thus, Dubensky et al. already provides motivation for following a prime and boost protocol to induce an antigen specific immune response. Dubensky et al. only differs from the instant invention as claimed by not teaching that protein antigen can be administered instead of the vector following the first vector administration.

Hu et al. was cited for teaching the benefits of "boosting" a live recombinant virus immunization with the immunizing protein itself instead of with a second immunization with the recombinant virus. Further, it is disagreed that either the abstract or Tables 1 or 2 somehow "teach away" from the use of a "non-replicating" versus a "replicating" virus. The Hu et al. reference does not in fact refer specifically to the replication status of the recombinant vaccinia virus encoding gp160, and in Table I, it is clear that immunization with a single dose of vaccinia virus encoding gp160, the "replicating" virus, does not induce greater amounts of antibody than administration of gp160 protein. Further, Table 1 provides motivation to boost with a protein rather than a second vector administration since Group 1, which received two

administrations of the viral vector generated less antigen specific antibody at week 10 than Group II which received the virus and then the gp160 protein itself.

Regarding the teachings of Paielli et al., this reference discusses the difference in the amount of viral DNA detected in animals transfected with either replication competent or incompetent adenoviral vector. This reference is silent in regards to vaccinia virus, and further does not teach any correlation, positive or negative, between immunization potential and replication competency. As noted above, Dubensky et al. already teaches that viral vector and layered eukaryotic vector initiation systems, regardless of replication competency, are useful for generating antigen specific immune responses. Finally, as applicant themselves note on page 8 of their response, the art-recognized adverse effects of generating viral specific immune responses in addition to antigen specific immune responses using replicating virus would further motivate the skilled artisan to utilize a non-replicating rather than a replicating virus to generate antigen specific immune responses in an animal.

Therefore, it is maintained that since Dubensky et al. teaches that both replicating and non-replicating alphaviruses and layered eukaryotic vector initiation systems can induce antigen specific immune responses and further teaches a "prime and boost" protocol using multiple vector administrations, and since Hu et al. teaches that boosting with protein is more effective than boosting with vector, it would have been *prima facie* obvious to the skilled artisan at the time of filing to utilize the prime boost approach taught by Hu et al. in the immunization methods of Dubensky et al. Further, based on the state of the art in generating immune responses using replicating and non-replicating viruses, the skilled artisan would have had a reasonable expectation of success in generating an immune response by administering a

"non-replicating" vector construct encoding a viral antigen followed or preceded by administration of the viral antigen itself.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (571) 272-0737. If the examiner is not available, the examiner's supervisor, Joseph Woitach, can be reached at (571) 272-0739. For all official communications, **the new technology center fax number is (571) 273-8300**. Please note that all official communications and responses sent by fax must be directed to the technology center fax number. For informal, non-official communications only, the examiner's direct fax number is (571) 273-0737. For any inquiry of a general nature, please call (571) 272-0547.

The applicant can also consult the USPTO's Patent Application Information Retrieval system (PAIR) on the internet for patent application status and history information, and for electronic images of applications. For questions or problems related to PAIR, please call the USPTO Patent Electronic Business Center (Patent EBC) toll free at 1-866-217-9197. Representatives are available daily from 6am to midnight (EST). When calling please have your application serial number or patent number available. For all other customer support, please call the USPTO call center (UCC) at 1-800-786-9199.

Dr. A.M.S. Wehbé

/Anne Marie S. Wehbé/
Primary Examiner, A.U. 1633